Fibrinolysis Versus Primary Percutaneous Intervention in ST-elevation Myocardial Infarction With Long Interhospital Transfer Distances

Address for correspondence:
Abhimanyu Beri, MD
B301 Clinical Center
138 Service Road
East Lansing, MI 48824
abhiberi@gmail.com

Abhimanyu Beri, MD; Mary Printz, FNP-BC; Ansar Hassan, MD, PhD; Joseph D. Babb, MD
Division of Internal Medicine, Michigan State University, (Beri), East Lansing, Michigan; Department of Cardiology, Pitt County Memorial Hospital, (Printz), Greenville, North Carolina; Department of Cardiac Surgery, Saint John Regional Hospital, Saint John, (Hassan), New Brunswick, Canada; Department of Cardiology, East Carolina University, (Babb), Greenville, North Carolina

ABSTRACT

Background: Current guidelines recommend rapid initiation of reperfusion therapy for ST-elevation myocardial infarction (STEMI), with short-distance transfer for primary percutaneous coronary intervention (pPCI) preferred over fibrinolysis in non–pPCI-capable hospitals. Comparative outcomes in patients with longer transfer times are unclear.

Hypothesis: We designed this study to assess whether administering fibrinolytics prior to initiating longer-distance interhospital transfer in patients with STEMI leads to a delay in transfer or worse outcomes compared with transfer for pPCI.

Methods: We analyzed 259 STEMI patients transferred to a receiving pPCI-capable center in eastern North Carolina. The patients were divided into 2 groups, with 43 (16.6%) transferred for pPCI and the remaining 216 (83.4%) transferred following fibrinolysis. The primary endpoint was door-to-door time. We also compared stroke, death, significant bleeding, and combined outcomes between the 2 groups.

Results: The median door-to-door time was similar for pPCI and fibrinolysis patients (135 vs 128 minutes; $P = 0.71$). Median door-to-balloon time among pPCI patients was 182 minutes from the point of arrival at the referral hospital and 49 minutes from arrival at the receiving pPCI center. Median door-to-needle time in the fibrinolysis patients was 30 minutes, with rescue PCI eventually performed in 81 (37.5%) patients. In-hospital mortality was higher in patients with pPCI (9.3%) compared with fibrinolysis patients (1.9%; $P = 0.03$). Combined incidence of stroke, significant bleeding, and death was 14% in pPCI patients compared with 7% in fibrinolysis patients ($P = 0.13$).

Conclusions: In settings with longer transfer distances, administering fibrinolytics prior to transfer to a pPCI-capable center did not cause any significant delay in transfer or worse outcomes.

Introduction

Rapid initiation of reperfusion therapy for ST-elevation myocardial infarction (STEMI) with either fibrinolytic therapy or primary percutaneous coronary intervention (pPCI) limits infarct size and improves survival.[1] The Door-to-Balloon (D2B) initiative sponsored by the American College of Cardiology (ACC) aims to improve patient care by reducing reperfusion times. The ACC/American Heart Association (AHA) guidelines recommend that chemical reperfusion with fibrinolytic therapy be instituted within 30 minutes or pPCI be performed within 90 minutes of presentation to the emergency department (ED).[1] Many regional networks have been established to improve reperfusion times in STEMI.[2–5] Studies involving most of these networks[6–11] have concluded that transfer for pPCI is superior to on-site fibrinolysis in patients requiring short (≤ 2 hours) interhospital transfers. However, 75% of STEMI patients throughout the United States (US) present to hospitals lacking the staff and resources to perform pPCI.[12] In addition, with more than 52% of the rural US population living more than 60 minutes from a pPCI facility, the achievement of a D2B time ≤ 90 minutes remains a logistical dilemma for these individuals.[13]

The Reperfusion of Acute Myocardial Infarction in Carolina Emergency Departments (RACE) initiative was established in North Carolina (NC) to streamline STEMI care.[2] In spite of significant reductions in transfer and reperfusion times in the entire state, the median D2B times in eastern NC remained greater than 2 hours.[14] The geographic limitations and long transfer distances

The authors have no funding, financial relationships, or conflicts of interest to disclose. This research work was performed at East Carolina University/Pitt County Memorial Hospital, Greenville, North Carolina.

Clin. Cardiol. 33, 3, 162–167 (2010)
Published online in Wiley InterScience. (www.interscience.wiley.com)
DOI:10.1002/clc.20723

Received: September 22, 2009
Accepted with revision: November 20, 2009

precluded achievement of the D2B targets set by the AHA/ACC, thus bringing into consideration a potential role for fibrinolytics as first-line reperfusion therapy in these patients. The purpose of this study was to assess whether administering fibrinolytics prior to initiating longer-distance interhospital transfers in STEMI patients led to a delay in transfer or worse outcomes when compared with direct transfer for pPCI.

Methods

Patient Population

Included in this analysis were patients with acute STEMI who were transferred from 14 non–pPCI-capable referral hospitals to Pitt County Memorial Hospital (PCMH), a 24-hour pPCI-capable receiving hospital in eastern NC, between December 2006 and June 2008 (Figure 1). STEMI was defined as the onset of angina or equivalent symptoms within 12 hours of presentation at the regional hospital and ST elevation (30.1 mV) in 2 or more contiguous leads or presumed new-onset left bundle branch block on electrocardiography (ECG). No patients were excluded from the analysis. The start date was chosen as December 2006 because the RACE intervention had been completed and protocols had already been established to ensure rapid transport and treatment of STEMI patients.[2,15]

All patients diagnosed with STEMI at referral hospitals were transferred to PCMH with priority, irrespective of whether they had received fibrinolytics or not. Intravenous fibrinolytics were administered at the discretion of the ED physicians to STEMI patients presenting at the referral hospitals. Standard contraindications to fibrinolysis were applied, including uncontrolled hypertension, malignant disease, recent major surgery or bleeding, prolonged cardiopulmonary resuscitation, and severe heart failure. Patients who underwent fibrinolysis received either full-dose tenecteplase (64.4%) or reteplase (35.6%) and were eligible for transfer immediately after completion of fibrinolysis. Those patients not qualifying for fibrinolytics or with very short ($\leq$ 30 minutes) anticipated transfer time were referred for pPCI. A single telephone call by the referring ED physician could activate the catheterization laboratory and staff at the pPCI hospital. The same telephone call also activated a mobile intensive care unit transport service to leave for the referral hospital. Interhospital patient transfer was provided mainly by this service (sites shown in Figure 1), as the majority of the counties had small hospitals and limited emergency medical service (EMS) resources. The mode of interhospital transportation (air or ground) was based on the estimated transport time and existing weather conditions. Helicopters were available for takeoff from 2 regional locations at <10 minutes' notice. The median distance to the receiving pPCI center from the referral hospitals was 52 miles (interquartile range [IQR], 38–69) with an average 1-way travel time of 72 minutes

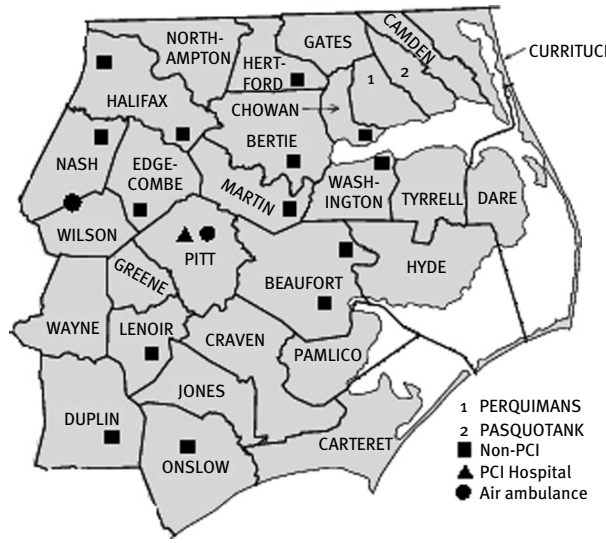

Figure 1. County map of eastern North Carolina showing locations of the pPCI-capable hospital (▲), non–pPCI-capable hospitals (■), and the two air ambulances (●). In addition to the counties with non–pPCI-capable hospitals, patients also were referred from the coastal counties without any hospitals. The total area shown on the map is approximately 14 670 square miles.

(IQR, 50–86) by ground (Supplementary Appendix 1). Air transport was preferred, weather permitting, given the long transfer distances in this region.

All patients arriving at PCMH had a "pit stop" evaluation in the ED by an interventional cardiologist to assess for successful reperfusion if they had already received fibrinolytics, or directly in the cardiac catheterization laboratory area if they had been transferred for pPCI. A protocol for rescue PCI was initiated if less than half of the ST elevation had resolved at the time of the first ECG at PCMH, or if typical anginal symptoms persisted. Full-dose fibrinolytic therapy was used with rescue PCI (if needed), rather than facilitated PCI with half-dose lytics.

Data Collection

Patient data were retrospectively collected using the information entered in the National Registry of Myocardial Infarction 5 (NRMI 5) and subsequently Acute Coronary Treatment and Intervention Outcomes Network (ACTION) registries. The NRMI 5 (December 2006–December 2007) and ACTION (January 2008–June 2008) protocols specified that all consecutive patients presenting at participating hospitals with diagnoses of 410.x1–410.x9 according to the International Classification of Diseases, 9th Revision (ICD-9) be enrolled in these registries. Patient demographics (eg, age, sex, body mass index) and information on presenting characteristics (eg, systolic blood pressure, pulse, and presence of shock or congestive heart failure)

were collected. In-hospital complications including stroke (both hemorrhagic and ischemic in origin), significant bleeding requiring transfusion, death, and need for rescue PCI were also recorded.

Endpoints

The primary endpoint, door-to-door (D2D) time, was defined as the time from arrival at the referred hospital to the arrival at the PCI center. The door-in-door-out time was measured from the patient's arrival to and departure from the referral hospital. Door-to-needle (D2N) time and D2B times were also calculated. Secondary endpoints included stroke, death, and significant bleeding, as well as combined events.

Statistical Analysis

Comparisons were made between patients transferred for pPCI and those transferred after fibrinolytic treatment. Proportions for categorical variables were compared using the χ^2 test and continuous variables analyzed using the Fisher exact test. Means were compared using ANOVA, and medians were compared using the Kruskal-Wallis statistic. Analyses were conducted using Microsoft SAS software (version 9.1.3). A P value of ≤ 0.05 was considered significant. The institutional review board at PCMH approved this study.

Results

Between December 2006 and June 2008, a total of 259 patients with STEMI were transferred from the non-pPCI referral hospitals to PCMH. Of these patients, 43 (16.6%) were transferred for pPCI, with the remaining 216 (83.4%) being transferred after fibrinolysis for further management. Their baseline characteristics are described in Table 1. The mean age of patients transferred for pPCI was 65.2 ± 13.5 years, compared with 58.7 ± 12.5 years for patients transferred after fibrinolysis. Congestive heart failure was more frequent in pPCI (20.9%) compared with fibrinolysis (3.7%; $P < 0.001$) patients, as was cardiogenic shock (14.0% vs 0.5%; $P < 0.001$).

Treatment time intervals are shown in Table 2. The median D2D time was 135 minutes (IQR, 109–170) for pPCI patients, compared with 128 minutes (IQR, 102–170; $P = 0.71$) in patients transferred following fibrinolysis. Median door-in-door-out times were similar in both groups (100 vs 84 minutes; $P = 0.45$). Times for transport from the referral hospital to PCMH were also similar (38 vs 44 minutes; $P = 0.29$).

Door-to-door-to-balloon in the pPCI group was 182 minutes (IQR, 128–230) and the D2B time was 49 minutes (IQR, 39–75) from the time of arrival at PCMH. Median D2N time in the fibrinolysis group was 30 minutes (IQR, 20–45 minutes), with 51.4% being performed in less than 30 minutes. In the fibrinolysis patients, rescue PCI had to be performed in 81 (37.5%) patients, and coronary stents were placed in 75 (92.6%) of these patients.

Table 1. Baseline Characteristics of Patients Transferred From Regional Non-pPCI Hospitals to a Tertiary, PCI Center for Further Care

Patient Characteristic	pPCI (n = 43)	Fibrinolytics (n = 216)	*P* Value
Age (± 2SD)	65.2 ± 13.5	58.7 ± 12.5	0.002
Age ≥ 75 y (%)	11 (25.6)	19 (8.9)	0.002
Female sex (%)	16 (37.2)	58 (26.9)	0.17
BMI (± 2SD)	29.0 ± 6.8	28.8 ± 5.5	0.83
BMI ≥ 30 (%)	14 (32.6)	78 (36.5)	0.63
Clinical features at presentation			
Systolic blood pressure (± 2SD)	127.8 ± 40.3	137.1 ± 29.1	0.07
Heart rate (± 2SD)	73.0 ± 20.4	77.6 ± 20.4	0.18
Heart failure (%)	9 (20.9)	8 (3.7)	< 0.001
Cardiogenic shock (%)	6 (14.0)	1 (0.5)	< 0.001
ST elevation[a] (%)	41 (95.4)	215 (99.5)	0.07

Abbreviations: BMI, body mass index; pPCI, primary percutaneous coronary intervention; SD, standard deviation.
[a]The remainder had presumed new-onset left bundle branch block.

In-hospital outcomes are described in Table 3. The incidence of in-hospital mortality was 9.3% in patients with pPCI compared with 1.9% in thrombolyzed patients ($P = 0.03$). Stroke occurred in 3 patients (1 was hemorrhagic) who underwent fibrinolysis compared with 0 patients in the pPCI group. Bleeding that warranted transfusion was noted in 4.6% of patients in each category. Combined incidence of stroke, significant bleeding, and death was 6 (14.0%) in pPCI patients compared with 15 (6.9%) in fibrinolysis patients ($P = 0.13$).

Discussion

Our study found that in a setting with long transfer distances, administering fibrinolytics prior to transfer from a non–pPCI-capable referral to a pPCI-capable receiving center did not cause any significant delay in transfer. We also found that patients who received fibrinolysis as an initial reperfusion strategy did not have overall worse outcomes (ie, major bleeding, stroke, death, or combined outcomes) compared with patients transferred for pPCI. Rescue PCI rates were not significantly different from those reported in previous studies.[4]

Table 2. Critical Time Intervals in Minutes Comparing Patients Transferred for pPCI Versus After Fibrinolytics

Time Interval	pPCI (n = 43)	Fibrinolytics (n = 216)	*P* Value
Onset of symptoms to arrival at peripheral hospital (median IQR)	83 (55–265)	95 (51–169)	0.71
Door-in-door-out time (median IQR)	100 (69–113)	84 (64–117)	0.45
Door-in-door-out ≤ 30 min (%)	1 (2.6)	3 (1.4)	0.49
Door-in-door-out ≤ 60 min (%)	8 (21.1)	46 (21.7)	0.93
Transfer out from peripheral hospital to arrival at PCI center (median IQR)	38 (25–68)	44 (29–62)	0.29
Door-to-door time (median IQR)	135 (109–170)	128 (102–170)	0.71
Door-to-door time ≤ 60 min (%)	1 (2.6)	0 (0.0)	0.15
Onset of symptoms to arrival at PCI center (median IQR)	216 (180–396)	246 (180–327)	0.88
D2N time (median IQR)	NA	30 (20–45)	NA
D2N time ≤ 30 min (%)	NA	111 (51.4)	NA
Door-to-door to balloon time (median IQR)	182 (128–230)	NA	NA
D2B time (median IQR)	49.0 (39.0–75.0)	NA	NA
D2B time ≤ 60 min (%)	33 (76.7)	NA	NA
D2B time ≤ 90 min (%)	39 (90.7)	NA	NA

Abbreviations: D2B, door-to-balloon; D2N, door-to-needle; IQR, interquartile range; NA, not applicable; pPCI, primary percutaneous coronary intervention.

Table 3. Comparison of In-hospital Clinical Outcomes Between Patients Transferred for pPCI Versus After Fibrinolysis

Outcome Measure	pPCI (n = 43)	Fibrinolytics (n = 216)	*P* Value
Death (%)	4 (9.3)	4 (1.9)	0.03
Stroke (%)	0 (0.0)	3 (1.4)	1
Hemorrhagic stroke (%)	0 (0.0)	1 (0.5)	1
Significant bleeding requiring blood transfusion (%)	2 (4.7)	10 (4.6)	1
Death, stroke, or significant bleeding (%)	6 (14.0)	15 (6.9)	0.13
Rescue PCI (%)	NA	81 (37.5)	NA

Abbreviations: NA, not applicable; PCI, percutaneous coronary intervention; pPCI, primary percutaneous coronary intervention.

Proponents of regionalizing STEMI care envision that a shift toward pPCI would either involve EMS to diagnose STEMI en route and determine whether transport to a pPCI-capable hospital is feasible, or would require interhospital transfers.[16] EMS-initiated direct transfer of STEMI patients to pPCI centers has been used and shown significant reduction in reperfusion times compared with short-distance interhospital transfers.[11,17,18] In regional networks with long-distance transfers, this could be adapted to direct STEMI patients within a certain radius to pPCI centers. Patients who are farther away (eg, >60 minutes) or lacking advanced EMS facilities could be initially sent for fibrinolysis to non-PCI hospitals with later interhospital transfer. The STAT Heart Program initiated in January 2005 in central Illinois showed that in rural US communities, ED physician-initiated interhospital transfer of STEMI patients for primary or rescue PCI was feasible and could be safely executed with achievement of timely reperfusion.[3] It also noted that two-thirds of their time was spent waiting for transport, suggesting the need for EMS activation of the interhospital transport system. Many other controlled studies have shown that interhospital transfers for STEMI can be used safely to achieve acceptable D2B times.[6–8]

However, whether acceptable D2B times may be achieved in uncontrolled settings has not been confirmed, as the reported median D2B time for patients transferred for pPCI in the US is 180 minutes, with only 4% being treated within 90 minutes.[19] Patients transferred to rural, teaching hospitals have substantially longer (≥ 1 hour) D2B times compared with patients transferred to urban, nonteaching

Published online in Wiley InterScience. (www.interscience.wiley.com)
DOI:10.1002/clc.20723

hospitals.[19] When interpreted within the context of national quality guidelines, these numbers suggest that transfer for pPCI in the US is presently failing to achieve established standards in the majority of STEMI patients. Excessive delays associated with interhospital transfer in the real-world setting may reduce the morbidity and mortality benefits seen in clinical trials, where patients are carefully selected for enrollment and delays in initiating treatment and transfers are minimized.

In our study, the staff and resources were optimized to ensure rapid transport of all STEMI patients as part of the RACE protocol. In spite of these efforts, we were still unable to achieve acceptable ($\leq$ 90 minutes) D2B times. This was secondary to the long transfer distances in our region between referral hospitals and the receiving pPCI-capable center.[14] As noted in previous studies,[3] due to the scarce availability of EMS at the referring centers for transport to the pPCI center, more than half of the door-in-door-out time was spent waiting for EMS arrival to transport the patients. Given these circumstances, we used fibrinolytics as a primary reperfusion strategy for eligible STEMI patients and found that this did not delay transfer to the regional pPCI center or result in worse outcomes. The Primary Angioplasty in Patients Transferred From General Community Hospitals to Specialized PTCA Units With or Without Emergency Thrombolysis (PRAGUE-2) and Comparison of Angioplasty and Prehospital Thrombolysis in Acute Myocardial Infarction (CAPTIM) trials[20,21] showed that in patients who could be reperfused within 2 to 3 hours of symptom onset, thrombolysis might be an equally good or better strategy than transfer for pPCI. Similar findings have been reported from the Danish Trial in Acute Myocardial Infarction 2 (DANAMI-2) trial that showed no significant difference in long-term all-cause and cardiac mortality between patients randomized to fibrinolysis or pPCI.[22] Although pPCI remains the optimal form of revascularization in STEMI patients with acceptable D2B times or those ineligible for fibrinolysis, primary therapy with fibrinolytics appears to have no adverse effect in patients with longer transfer times and may lead to better outcomes.

Study Limitations

Our results should be interpreted cautiously, as this is a single-center observational analysis. Given the financial and geographic limitations of our region, our findings may not be extrapolated to other areas. There was a significant difference between the fibrinolysis and pPCI cohorts. Lastly, there may have been a selection bias, with a higher percentage of patients with heart failure and related cardiogenic shock in the primary PCI group compared to the fibrinolysis group. This may have confounded our results and led to sicker patients being designated for direct transfer rather than to receive thrombolytics, and this could have had delayed transfer.

Conclusion

In a real-world setting with long transfer distances, we found that administering fibrinolytics did not delay patient transfer to a tertiary center or lead to significantly adverse outcomes compared with pPCI. On-site fibrinolytic therapy remains a very practical option for reperfusion in a large subset of patients who are expected to have long transfer times. Transfer for pPCI remains the preferred reperfusion strategy for patients with contraindications to fibrinolysis.

References

1. Antman EM, Hand M, Armstrong PW, et al. 2007 focused update of the ACC/AHA 2004 guidelines for the management of patients with ST-elevation myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines [published correction appears in *J Am Coll Cardiol*. 2008;51:977]. *J Am Coll Cardiol*. 2008; 51:210–247.
2. Jollis JG, Roettig ML, Aluko AO, et al; for Reperfusion of Acute Myocardial Infarction in North Carolina Emergency Departments (RACE) Investigators. Implementation of a statewide system for coronary reperfusion for ST-segment elevation myocardial infarction. *JAMA*. 2007;298:2371–2380.
3. Aguirre FV, Varghese JJ, Kelley MP, et al; for STAT Heart Investigators. Rural interhospital transfer of ST-elevation myocardial infarction patients for percutaneous coronary revascularization: the STAT Heart Program. *Circulation*. 2008;117: 1145–1152.
4. Ting HH, Rihal CS, Gersh BJ, et al. Regional systems of care to optimize timeliness of reperfusion therapy for ST-elevation myocardial infarction: the Mayo Clinic STEMI protocol. *Circulation*. 2007;116:729–736.
5. Khot UN, Johnson ML, Ramsey C, et al. Emergency department physician activation of the catheterization laboratory and immediate transfer to an immediately available catheterization laboratory reduce door-to-balloon time in ST-elevation myocardial infarction. *Circulation*. 2007;116:67–76.
6. Andersen HR, Nielsen TT, Rasmussen K, et al. A comparison of coronary angioplasty with fibrinolytic therapy in acute myocardial infarction. *N Engl J Med*. 2003;349:733–742.
7. Grines CL, Westerhausen DR Jr, Grines LL, et al; for Air PAMI Study Group. A randomized trial of transfer for primary angioplasty versus on-site thrombolysis in patients with high-risk myocardial infarction: the Air Primary Angioplasty in Myocardial Infarction study. *J Am Coll Cardiol*. 2002;39:1713–1719.
8. Le May MR, Davies RF, Dionne R, et al. Comparison of early mortality of paramedic-diagnosed ST-segment elevation myocardial infarction with immediate transport to a designated primary percutaneous coronary intervention center to that of similar patients transported to the nearest hospital. *Am J Cardiol*. 2006;98:1329–1333.
9. Keeley EC, Boura JA, Grines CL. Primary angioplasty versus intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review of 23 randomised trials. *Lancet*. 2003;361:13–20.
10. Boersma E; for the Primary Coronary Angioplasty vs. Thrombolysis Group. Does time matter? A pooled analysis of randomized clinical trials comparing primary percutaneous coronary intervention and in-hospital fibrinolysis in acute myocardial infarction patients. *Eur Heart J*. 2006;27:779–788.

Published online in Wiley InterScience. (www.interscience.wiley.com)
DOI:10.1002/clc.20723

11. Le May MR, So DY, Dionne R, et al. A citywide protocol for primary PCI in ST-segment elevation myocardial infarction. *N Engl J Med*. 2008;358:231–240.
12. Jacobs AK, Antman EM, Faxon DP, et al. Development of systems of care for ST-elevation myocardial infarction patients: executive summary [published correction appears in *Circulation*. 2007;116:e77]. *Circulation*. 2007;116:217–230.
13. Nallamothu BK, Bates ER, Wang Y, et al. Driving times and distances to hospitals with percutaneous coronary intervention in the United States: implications for prehospital triage of patients with ST-elevation myocardial infarction. *Circulation*. 2006;113: 1189–1195.
14. Beri A, Hassan A, Printz M, et al. Long-term impact of a regional network for treatment of ST elevation myocardial infarction [abstract]. *Circ Cardiovasc Qual Outcomes*. 2009;2: A152.
15. Jollis JG, Mehta RH, Roettig ML, et al. Reperfusion of acute myocardial infarction in North Carolina emergency departments (RACE): study design. *Am Heart J*. 2006;152:851.e1–851.e11.
16. Rokos IC, Larson DM, Henry TD, et al. Rationale for establishing regional ST-elevation myocardial infarction receiving center (SRC) networks. *Am Heart J*. 2006;152:661–667.
17. van't Hof AW, Rasoul S, van de Wetering H, et al; for On-TIME Study Group. Feasibility and benefit of prehospital diagnosis, triage, and therapy by paramedics only in patients who are candidates for primary angioplasty for acute myocardial infarction. *Am Heart J*. 2006;151:1255.e1–1255.e5.
18. Terkelsen CJ, Lassen JF, Norgaard BL, et al. Reduction of treatment delay in patients with ST-elevation myocardial infarction: impact of pre-hospital diagnosis and direct referral to primary percutaneous coronary intervention. *Eur Heart J*. 2005;26:770–777.
19. Nallamothu BK, Bates ER, Herrin J, et al; for NRMI Investigators. Times to treatment in transfer patients undergoing primary percutaneous coronary intervention in the United States: National Registry of Myocardial Infarction (NRMI)-3/4 analysis. *Circulation*. 2005;111:761–767.
20. Widimský P, Buděšínský T, Voráč D. Long distance transport for primary angioplasty vs immediate thrombolysis in acute myocardial infarction: final results of the randomized national multicentre trial—PRAGUE-2. *Eur Heart J*. 2003;24:94–104.
21. Steg PG, Bonnefoy E, Chabaud S, et al; for CAPTIM Investigators. Impact of time to treatment on mortality after prehospital fibrinolysis or primary angioplasty: data from the CAPTIM randomized clinical trial. *Circulation*. 2003;108:2851–2856.
22. Nielsen PH, Maeng M, Busk M, et al; for DANAMI-2 Investigators. Primary angioplasty versus fibrinolysis in acute myocardial infarction: long-term follow-up in the DANAMI-2 Trial [abstract]. *J Am Coll Cardiol*. 2009;53(Suppl. 2suppl 1):A459.

Published online in Wiley InterScience. (www.interscience.wiley.com)
DOI:10.1002/clc.20723